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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/661,905 | 09/12/2003 | Ji-In Kim Almstead | 8543D | 9381 |

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| EXAMINER | |
|---|---|
| KWON, BRIAN YONG S | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/661,905 | ALMSTEAD ET AL. | |
| | Examiner | Art Unit | |
| | Brian S. Kwon | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

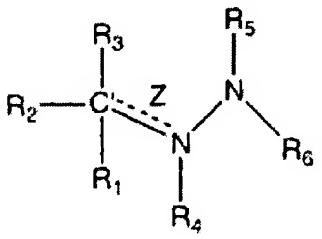
### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-5 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of increasing erythropoietin in a mammal comprising administering a compound of the structure represented by




The instant specification provides assay technique (Example VI) to test the compounds in vitro and discloses that any compound of the present invention can be further tested in vivo for its ability to increase EPO protein levels in rat model. However, there is no demonstrated tests and/or results (in the form of data) in the specification for the skilled artisan to recognize that the applicant was contemplated of the claimed invention.

Although the specification discloses in Example A that the oral administration of table composition comprising compound of Example 2 was found to increase EPO in a subject suffering from anemia. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential assaying method of measuring increased EPO protein level. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented

what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

2. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for said method with the administration of compound of Example 2 (N-pyridin-2-yl-N'-(1-pyridin-2-yl-ethylidene)hydrazine), does not reasonably provide enablement for "a compound of the structural formula" or "other species of the compound of the structural formula". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The claims are directed to a method for increasing erythropoietin in a mammal comprising administering the compound of said structural formula.

Said compound(s) represented by the formula is/are known to have anticonvulsant, antifungal and factor XA inhibitor (US 5942527; US 6329378; WO 2002016315). However, the state of the art does not recognize their activity in increasing erythropoietin in mammal. Nor, there are known compounds of similar structure which have been demonstrated to exhibit the claimed activity.

As discussed above, since the state art is silent about the claimed utility of said compounds, the skilled artisan must rely on evidence provided in the specification that the applicant's assertion has merits.

The relative skill or unpredictability of those in the art of pharmaceuticals is high. The specification does not provide any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instantly claimed compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims covers plethora of compounds (over 1000 compounds) represented by the formula. Possible substituents according to the formula include "aryl, cycloalkyl, heteroaryl or heterocyloalkyl" in R1 and R6.

In the instant case, compounds of the Example 2 (N-pyridin-2-yl-N'-(1-pyridin-2-yl-ethylidene)hydrazine), Example 3 (N-methyl-N-pyridin-2-yl-N'-pyridin-2-ylmethylene-hydrazine) and Example 15 ((N-1-pyridin-2-yl-N'-ethylidene)-N-(9H-

1,3,4,9-tetraza-fluoren-2-yl)-hydrazine) are disclosed as working examples, but the compound of the Example 2 was only tested for its efficacy in increasing erythropoietin in a subject having anemia. As discussed above, very limited numbers of the compounds are set forth as working examples. It is noted that these examples are neither exhaustive, nor define the class of condition required.

Although the specification provide sufficient guidance in how to make/screen potential compounds that are suitable for the claimed invention (page 26-28 of the specification), the specification fails to provide sufficient clarity in how to use it. The specification provides no guidance, in the way of enablement for the full scope of all compounds that are potentially suitable for the invention work similarly as to the compound of Example 2. The skill artisan would have not known that which compounds of the claimed compounds are capable of accomplishing the desired result of the claimed invention **without undue amount of experimentation**.

As discussed above, although the specification provide enabling disclosure for increasing erythropoietin with the Example 2 compound, none of the specification provides enabling disclosure for the full scope of all compounds that may not have similar activity as the tested compound. There is no demonstrated correlation that the tests and results apply to the claimed utility embraced by the instant claims.

Since the efficacy of said compounds in increasing erythropoietin mentioned above cannot be predicted from a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to use the invention commensurate in scope with the claims.

## Conclusion

3. No Claim is allowed.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614